

**REMARKS**

Reconsideration and withdrawal of the rejections and objections of the application are respectfully requested in view of the remarks herewith, which place the application into condition for allowance.

**I. Status of the Claims and Formal Matters**

In response to the Office Action mailed December 18, 2009<sup>1</sup>, Claims 28-29 stand pending. Claim 28 is herein amended. As amended, Claims 28-29 thus stand pending. Support for these amendments may be found generally throughout the specification inclusive and more specifically within the originally filed claims, Tables I and II, and paragraph 38 of the specification. No new matter has been added by virtue of these amendments.

Applicants expressly state that the claims, as amended, are intended to include and encompass the full scope of any equivalents as if the claims had been originally filed and not amended. Thus, Applicants hereby expressly rebut any presumption that Applicants have narrowed or surrendered any equivalents under the doctrine of equivalents by amending the claims, or by presenting any remarks in this paper, and in no way do Applicants disclaim any of the territory between the original claims and the amended claims with respect to any equivalent subject matter.

Applicants expressly reserve the right to file a divisional and/or continuation application claiming the non-elected subject matter.

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<sup>1</sup> Applicants respectfully note that the previous office action (Final Office Action of May 5, 2009) did not cite any references against the then pending claims (Claims 1-27). Accordingly, Applicants arguments contained in the RCE and Preliminary Amendment filed September 24, 2009 did not compare the newly presented claims (Claims 28-29) therein to any references, as there were no cited references to compare said new claims against.

## II. Claim Rejections

### A) 35 USC § 112, 2<sup>nd</sup> paragraph

Claims 28-29 stand rejected under 35 U.S.C. 112, 2<sup>nd</sup> paragraph, as being allegedly indefinite with regard to several claim terms. Applicants respectfully traverse and overcome this rejection based on the reasons stated below.

- 1) First, with regard to culture media, the Examiner alleges the ProCHO4-CDM media description is unclear as all ingredients of the media are not specified or readily made available. Applicants respectfully traverse and overcome this rejection based on the reasons stated below.

Applicants have amended Claim 28 to delete the reference to the ProCHO4-CDM media. Accordingly, Applicants respectfully submit that the 112, 2<sup>nd</sup> paragraph rejection to this claim term has been obviated.

- 2) Second, the Examiner has alleged indefiniteness regarding the claimed DMEM/Ham's F-12 media as to whether the culture is done in either media or in some mixture of both DMEM and Ham. Applicants respectfully traverse and overcome this rejection based on the reasons stated below.

Applicants have amended Claim 28 to clarify that the culturing of the CHO cell is done in either DMEM or Ham's F-12 media. Accordingly, Applicants respectfully submit that the 112, 2<sup>nd</sup> paragraph rejection to this claim term has been obviated.

- 3) Third, the Examiner alleges that the feeding glucose terms ("when the viable cell count is 1.8\*10<sup>6</sup> cells/ml or more", and "a constant glucose concentration (CGC)") are unclear as to which volume the "cells/ml" limitation refers, and to whether the CGC refers to the concentration of glucose in the solution being fed or the concentration of glucose in culture after addition. Applicants respectfully traverse and overcome this rejection based on the reasons stated below.

Applicants have amended Claim 28 to first, clarify the volume to which the cells/ml refers is the ml of media (in the reaction vessel), as one of ordinary skill in the art would know, and second to clarify that the CGC reference to the concentration of glucose in the feed (as shown in the Tables and Examples). Accordingly, Applicants respectfully submit that the 112, 2<sup>nd</sup> paragraph rejection to these claim terms have been obviated.

4) Finally, the constant flow rate "from D=0.03/h to D=0.05/h" is alleged to be indefinite for both D and the units for the numerical values. Applicants respectfully traverse and overcome this rejection based on the reasons stated below.

Applicants have amended Claim 28 to further define D, specifically that D refers to the volume flux of the feed added to the vessel (see for example paragraph 38 of the specification) and is expressed in units that reflect the volume flow in ml/h divided by the total media volume. This division, as one skilled in the art would appreciate, results in a normalized value that shows flow independent of volume. Accordingly, Applicants respectfully submit that one of ordinary skill in the art would readily comprehend this normalized value and that the term, as such, is not indefinite. Therefore Applicants respectfully submit that the 112, 2<sup>nd</sup> paragraph rejection to this claim term has been obviated.

Based on the above amendments, Applicants respectfully submit that the above indefinite rejections have been obviated and as such respectfully request that the 112, 2<sup>nd</sup> paragraph rejections be withdrawn and Claims 28-29 be placed into condition for allowance.

**B) 35 USC 103(a)**

Claims 28 and 29 are rejected under 35 USC 103(a) as obvious over Folena-Wasserman et al over Keen et al. For this rejection, the Examiner has interpreted Claims 28-29 as a method for producing an antibody comprising culturing CHO cells in

media at a pH between 6.7-7.7; measuring viable cell count; feeding glucose at some constant rate when the cell count reaches  $1.8 \times 10^6$  cells/mL medium or more; and recovering the antibody produced by the CHO cells, with the concentration of glucose in the medium maintained at about 24mmol/L, i.e., 4.3 g/L. Applicants respectfully traverse and overcome this rejection, as the combination of the two references do not clearly teach, disclose or suggest all the claimed elements of Applicants' invention.

Folena-Wasserman et al. (US 5,252,216) allegedly discloses a method for the cultivation of cells, in which, as the Examiner acknowledges on page 7 of the Office Action, the aim is to provide a constant glucose concentration inside the cultivation vessel, i.e. in the cultivation medium. As outlined in column 11, line 45, the method according to Folena-Wasserman is a "continuous perfusion process". In lines 67 following it is outlined that "medium perfusion was initiated, with periodic increases in (feeding) rates so as to maintain the glucose concentration (inside the reaction vessel constant) at 1.0 g/L". From this sentence it can be seen that the method reported in Folena-Wasserman is clearly different from the current method in at least the two essential points of:

i) the glucose concentration is kept constant in the reaction vessel – in direct contrast to Applicants invention which reports and explicitly requires/claims that the glucose concentration in the feed is kept constant. As can be seen from Tables 1 and 2 of the current invention the glucose concentration in the reaction vessel is decreasing until it's below the detection limit (denoted as "-" in the table). Thus, in Applicants claimed invention, the glucose concentration inside the reaction vessel is not kept constant; instead, and contrary to the teachings of Folena-Wasserman, it is decreasing.

ii) the feed is periodically increased – in contrast to the current invention wherein the feed is kept constant. This can be seen for example from the fact that the D value,

which denotes the media flow rate (paragraph [0038]), is kept constant as can be seen from the tables presented in the current specification.

The addition of Keen does not remedy this deficiency and teaching away of Folena Wasserman. Keen et al. (US 5,316,968) are completely silent about constant glucose concentration in the reaction vessel or a feeding strategy for the cultivation. Thus, Keen does not provide the missing claimed elements between Folena-Wasserman and the current invention, nor does Keen address the teaching away of Folena-Wasserman regarding the feed and the glucose concentration. As such, the combination of the two cited references would not lead one of ordinary skill in the art to change the glucose concentration and the feed from the teachings of Folena-Wasserman to Applicants claimed invention.

Accordingly, Applicants respectfully submit that the above obviousness rejection to Claims 28-29, as herein amended, have been obviated and as such respectfully request that the 35 U.S.C. 103(a) rejection be withdrawn and Claims 28-29 be placed into condition for allowance.

No further fee is required in connection with the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

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/Robert P. Hoag/  
Attorney for Applicant(s)  
Robert P. Hoag  
(Reg. No. 39712)  
340 Kingsland Street  
Nutley, NJ 07110  
Telephone (973) 235-4453  
Telefax: (973) 235-2363